

Amendments to the Claims

Please amend the pending claims with the following amended claims.

1 - 4. (Canceled)

5. (Currently Amended) A method for predicting a phospholipidosis induction potential of a test compound, which comprises

(1) determining ~~at~~ the standard value for the judgment of the presence or absence of a phospholipidosis induction potential of the test compound, which comprises:

(a) exposing samples containing mammalian cells to each of two or more compounds known to induce phospholipidosis and two or more compounds known not to induce phospholipidosis;

~~(a)(b)~~ detecting expression variation of a set of genes set forth as SEQ ID NOs:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21 and 23, in individual samples, ~~containing a mammalian cell exposed to each of two or more known phospholipidosis-inducing compounds and two or more known phospholipidosis non-inducing compounds, and~~

(c) taking a fold change of the expression amount of each gene as an expression variation rate (X) of the gene when the expression amount increased upon exposure and taking an inverse number of fold change of the expresstion amount of each gene as an expression variation rate (X) of the gene when the expression amount decreased upon exposure,

(d) calculating an average value of the expression variation rates of the 12 genes according to the following formula and determining as an average expression variation rate for each compound:

[average expression variation rate] = $m_1X_1 + m_2X_2 + \dots + m_{12}X_{12}$

($m_1 + m_2 + \dots + m_{12} = 1$),

wherein X_i ($i=1-12$) is the expression variation rate of each gene, m_i ($i=1-12$) is the weight of each gene and $m_i \times 12 = 0.2-5$;

- ~~(b)(e)~~ usingdetermining, as athe standard value, an cut-off value of average variation rate capable of correctly judging the presence or absence of a phospholipidosis induction potential of the above-mentioned compounds known to induce or not to induce phospholipidosis with the probability of
not less than about 70% based on the relationship between an average expression variation rate of the genes and the phospholipidosis induction potential; and
- (2) predicting a phospholipidosis induction potential of the test compound, which comprises:
- (a) detecting expression variation of a set of genes set forth as SEQ ID NOs:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21 and 23, in a sample containing the mammalian cell exposed to the test compound, and
- ~~(b)~~ calculating an average value of the expression variation rates of the 12 genes according to the formula shown in the step (1)(c) and determining as the average expression variation rate for the test compound,
- ~~(b)(c)~~ comparing the average expression variation rate for the test compound of gene expression with the standard value obtained by the step (1); and
- ~~(d)~~ predicting that the test compound has a phospholipidosis induction potential when the average expression variation rate for the test compound is not less than the standard value.

6 - 8. (Canceled)

9. (Currently Amended) The method of claim 5, wherein the step (1) further comprises examining validity of the standard value comprising the following steps:

- (e) detecting expression variation of a set of genes set forth as SEQ ID NOs:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21 and 23 in a sample containing the mammalian cells exposed to a compound known to induce or not to induce phospholipidosis other than those used in the step (1)(a),
- (f) comparing the average expression variation rate(s) for the compound with the standard value obtained by the step (1)(e), and

(g) evaluating that the standard value is valid when the presence or absence of a phospholipidosis induction potential of the compound is correctly judged based on the standard value.

~~examining validity of the standard value using other known phospholipidosis inducing compound and known phospholipidosis non-inducing compound.~~

10 - 11. (Canceled)

12. (Currently Amended) The method of claim 5, wherein the ~~phospholipidosis-inducing compound~~ known to induce phospholipidosis produces a myelin-like structure in the mammal cell.

13. (Currently Amended) The method of claim 12, wherein the ~~phospholipidosis-inducing compound~~ known to induce phospholipidosis is selected from the group consisting of amitriptyline, chlorcyclizine, fluoxetine, amiodarone, AY-9944, chlorpromazine, imipramine, tamoxifen, perhexiline, clozapine, sertraline, clomipramine, thioridazine, zimelidine, ketoconazole, loratadine and pentamidine.

14. (Currently Amended) The method of claim 5, wherein the ~~known phospholipidosis non-inducing compound~~ known not to induce phospholipidosis is selected from the group consisting of acetaminophen, clarithromycin, disopyramide, erythromycin, flecainide, haloperidol, levofloxacin, ofloxacin, procainamide, quinidine, sotalol, sulfamethoxazole and sumatriptan.

15. (Currently Amended) The method of claim 5, wherein ~~the average variation rate is following formula:~~

$$\text{Average variation rate} = m_1 X_1 + m_2 X_2 + \dots + m_n X_n$$

~~wherein X is an expression variation rate of each gene, n is the total number of genes, $m_1 + m_2 + \dots + m_n = 1$ and $m_i (i = 1 - 12) = 1/12n$.~~

16. (Currently Amended) The method of claim 5, wherein the phospholipidosis is induced in an organ or tissue ~~derived from~~ which the mammalian cell ~~to be~~ exposed to the test compound is derived.